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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MUETING, RAASCH & GEBHARDT, P.A.
P.O. BOX 581415
MINNEAPOLIS, MN 55458

EXAMINER	
AFREMOVA, VERA	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,867	STEER ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,23-30,33-42,44-54 and 66-75* is/are pending in the application.

4a) Of the above claim(s) *5,6,9-14,23-30,33-42,44-54 and 69-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,8,15-19 and 66-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/25/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19, 23-30, 33-42 and 44-54 as amended (12/13/2007) and new claims 66-75 (12/13/2007) are presently pending.

Claims 20-22, 31, 32, 43 and 55-65 were canceled by applicants (12/13/2007).

Election/Restrictions

Applicant's election with traverse of the group I-A, drawn to ***in vitro*** treatment of cells with hydrophilic bile acid in the reply filed on 12/13/2007 is acknowledged.

The traversal is on the ground(s) that there is no serious burden in searching and examining all pending claims including newly added claims. These arguments are not found persuasive because this application a 371 type of application and it contains claims drawn to more than one of permissible combinations of invention categories such as more than one of methods of using the hydrophilic bile acids or ursodeoxycholic acid (UDCA) for treating cells and for treating various patients. The corresponding special technical features such as the use of UDCA for treating cell populations and for administration to patients are known in the prior art. For example: see abstract of the reference by Rodrigues et al. (IDS reference; Journal of Clinical Investigation. June 1998. Vol. 101, No. 12, pages 2790-2799) that teaches the use of hydrophilic bile acid compounds including UDCA for treating liver cells and for administration to prevent cell apoptosis and cell alterations. Thus, the claimed inventions lack unity.

In response to the prior restriction requirement the original claims were considerably amended (12/13/2007), new claims were added (12/13/2007) and some claims were canceled (12/13/2007). Thus, for the clarity of the record of the instant prosecution the grouping of presently pending claims (as amended and new) is once again explained below.

Group I-A, amended pending claim(s) 1-4, 7-8, 15-19 and new claims 66-68, as drawn to an ***in vitro*** method of making a transplant cell population and promoting its viability by ***in vitro*** treatment of cells with ursodeoxycholic acid (UDCA) or its analog.

Group I-B, amended pending claim(s) 1-3, 5, 6, 9-19, drawn to an ***in vivo*** method of administration of ursodeoxycholic acid (UDCA) or its analog in the method for promoting transplant viability.

Group II, original claim 22 is canceled.

Group III, pending claim(s) 23-30, 33-41 as amended and new claims 69-71 and 75, drawn to a method of ***in vivo*** treating a subject with Parkinson's disease by transplanting cells treated with ursodeoxycholic acid.

Group IV, original claim(s) 42 and 44-53, drawn to a method of ***in vivo*** treating a donor of transplant cell population with hydrophilic bile acid.

Group V, original claims 54 and new claims 72 and 73, drawn to a method for ***in vivo*** treating a recipient of transplant cell population with hydrophilic bile acid.

The presently pending claims 5, 6, 9-14, 23-30, 33-42, 44-54, 69-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups of inventions that are all directed to non-elected ***in vivo*** treatment of cells and/or patients with hydrophilic bile acid or UDCA, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 12/13/2007. Applicants also argue that all new claims 66-75 and the amended claims 9-14 are linking to the in vitro method of treating cells with UDCA. This is not found convincing since new claims 69-75 and amended claims 9-14 are clearly directed to different invention categories such as more than one of

methods of using different products including product such as the hydrophilic bile acids or ursodeoxycholic acid (UDCA) in different in vivo environment(s) and including products such as cellular products-obtained-by treatment methods. With respect to claim 8 it is noted that is directed to an intended use but it does not recite any active step(s) and, thus, it remains in the elected group for the instant prosecution.

Claims 1-4, 7-8 and 15-19 as amended and new claims 66-68 as solely drawn to an ***in vitro*** method of making a transplant cell population and promoting its viability by ***in vitro*** treatment of cells with ursodeoxycholic acid (UDCA) or its analog are under examination in the instant office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7, 8, 15-19, 66 and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Falasca et al. (IDS reference; "Protective role of tauroursodeoxycholate during harvesting and cold storage of human liver". Transplantation. May 2001, Vol. 71, No. 9, pages 1268-1276).

Claims are directed to a method of making a transplant cell population and promoting its viability wherein the method comprises one active step of *in vitro* treatment of cells of the transplant cell population with ursodeoxycholic acid (UDCA) or its salts or its analog. Some claims are further drawn to the cells of the transplant cell population being differentiated or

precursor cells, to the cells of the transplant cell population being organ such as liver; or the cells of the transplant cell population being autologous, heterologous or xenologous tissues. Some claims are further drawn to contacting cells with the compound in combination with pharmaceutically acceptable carrier. Some claims are further drawn to contacting the cells with the UDCA analog such as tauroursodeoxycholic acid (TUDCA).

The reference by Falasca et al. teaches a protective role of tauroursodeoxycholate during harvesting and cold storage of human liver intended for transplantation. The cited reference discloses a method making a transplant cell population and promoting its viability wherein the method comprises one active step of *in vitro* treatment of human liver cells with TDCA or analog UDCA (entire document including abstract and page 1269, col. 2, par. 5). The compound TUDCA is in UW solution and, thus, in combination with a pharmaceutically acceptable carrier. The disclosed liver organ contains both differentiated hepatocytes as well as at least some undifferentiated precursor cells or adult stem cells within the broadest meaning of the claims when read in the light of instant specification (page 9, line 3).

Thus, the cited method comprises identical active step and identical structural elements as required by the claimed method and, therefore, the cited reference anticipates the claimed invention.

Claims 1-4, 7, 8, 15-17 and 66-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Rodrigues et al. (IDS reference; "Tauroursodeoxycholic acid partially prevents apoptosis induced by 3-nitropropionate acid: evidence for mitochondrial pathway independent of the permeability transition". Journal of Neurochemistry. 2000, Vol. 75, pages 2368-2379).

Claims are directed to a method of making a transplant cell population and promoting its viability wherein the method comprises one active step of *in vitro* treatment of cells of the transplant cell population with ursodeoxycholic acid (UDCA) or its salts or its analog. Some claims are further drawn to the cells of the transplant cell population being differentiated or precursor cells, to the cells being neuronal cells; or the cells of the transplant cell population being autologous, heterologous or xenologous tissues. Some claims are further drawn to contacting cells with the compound in combination with pharmaceutically acceptable carrier. Some claims are further drawn to contacting the cells with the UDCA analog such as tauroursodeoxycholic acid (TUDCA).

The reference by Rodrigues et al teaches that TUDCA prevents apoptosis in both hepatic and nonhepatic cells including neuronal cells. The cited reference discloses a method for making cells suitable for transplant and for promoting their viability wherein the method comprises one active step of *in vitro* treatment of hepatic and neuronal cells with TUDCA (entire document including abstract, page 2369, col. 2, paragraphs 3-4; Fig. 1; Fig. 6; etc.). The disclosed rat neuronal cell populations contain both differentiated and precursors cells in light of disclosure about further neuronal differentiation (page 2369, col. 2, par. 3, line 11). The compound TUDCA is dissolved in the cell culture medium and, thus, in combination with a pharmaceutically acceptable carrier. Therefore, the cited method comprises identical active step and identical structural elements as required by the claimed method and, thus, the cited reference anticipates the claimed invention.

Claims 1-4, 7, 8, 15-17 and 66-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Silva et al. ("Bilirubin induced apoptosis in rat cultured neural cells is aggravated by chenodeoxycholic acid but prevented by ursodeoxycholic acid". Journal of Hepatology. 2001, Vol. 34, pages 402-408).

Claims are directed to a method of making a transplant cell population and promoting its viability wherein the method comprises one active step of *in vitro* treatment of cells of the transplant cell population with ursodeoxycholic acid (UDCA) or its salts or its analog. Some claims are further drawn to the cells of the transplant cell population being differentiated or precursor cells, to the cells being neuronal cells; or the cells of the transplant cell population being autologous, heterologous or xenologous tissues. Some claims are further drawn to contacting cells with the compound in combination with pharmaceutically acceptable carrier. Some claims are further drawn to contacting the cells with the UDCA conjugated derivative or analog such as tauroursodeoxycholic acid (TUDCA).

The reference by Silva et al teaches that UDCA and its conjugated derivative TUDCA prevents cell death or of neuronal cells. The cited reference discloses a method for making cells suitable for transplant and for promoting their viability wherein the method comprises one active step of *in vitro* treatment of neuronal cells with UDCA and TUDCA (entire document including abstract; page 403, col. 2, par. 2; Fig. 4; page 406, col. 1, lines 6-9; etc.). The disclosed rat neuronal cell populations were isolated from embryonic tissue (page 403, col. 2, par. 2) and, thus, contain both differentiated and precursors cells within the broadest meaning of the instant claims and when read in the in light of instant specification (page 18, line 27-28). The compounds UDCA and TUDCA are dissolved in the cell culture medium and, thus, in

combination with a pharmaceutically acceptable carrier. Therefore, the cited method comprises identical active step and identical structural elements as required by the claimed method and, thus, the cited reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-8, 15-19 and 66-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falasca et al. (IDS reference; "Protective role of tauroursodeoxycholate during harvesting and cold storage of human liver". Transplantation. May 2001, Vol. 71, No. 9, pages 1268-1276), Rodrigues et al. (IDS reference; "Tauroursodeoxycholic acid partially prevents apoptosis induced by 3-nitropropionate acid: evidence for mitochondrial pathway independent of the permeability transition". Journal of Neurochemistry. 2000, Vol. 75, pages 2368-2379) and Silva et al. ("Bilirubin induced apoptosis in rat cultured neural cells is aggravated by chenodeoxycholic acid but prevented by ursodeoxycholic acid". Journal of Hepatology. 2001, Vol. 34, pages 402-408).

Claims are directed to a method of making a transplant cell population and promoting its viability wherein the method comprises one active step of *in vitro* treatment of cells of the transplant cell population with ursodeoxycholic acid (UDCA) or its salts or its analog. Some claims are further drawn to the cells of the transplant cell population being differentiated or

precursor cells, to the cells of the transplant cell population being organ such as liver; to the cells of the transplant cell population being neuronal cells; or the cells of the transplant cell population being autologous, heterologous or xenologous tissues. Some claims are further drawn to contacting cells with the compound in combination with pharmaceutically acceptable carrier. Some claims are further drawn to contacting the cells with the conjugated UDCA analog such as tauroursodeoxycholic acid (TUDCA).

The cited references Falasca et al., Rodrigues et al. and Silva et al. are relied upon as explained above and they teach protective role of UDCA and TUDCA for various mammalian cells including hepatic cells and neuronal cells and including organs.

In particular, Falasca et al discloses a method for making liver organ transplant by treating harvested organ with UDCA analog or with TUDCA but it is lacking particular disclosure about neuronal cells. However, the cited references by Rodrigues et al. and by Silva et al. teach that UDCA and TUDCA protect various mammalian cells including hepatic cells and neuronal cells from cell death or apoptosis.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was to use UDCA and/or TUDCA for in vitro treatment of various mammalian organs and cells including neuronal cells with a reasonable expectation of success in making transplant cell populations and promoting their viability because the prior art teaches and suggests protective role of UDCA and TUDCA for various mammalian cells including hepatic cells and neuronal cells and including organs. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1657

March 13, 2008

VERA AFREMOVA

PRIMARY EXAMINER

/Vera Afremova/
Primary Examiner, Art Unit 1657